Case reports

Beneficial effects of intravenous glyceryl trinitrate in a case of Prinzmetal angina

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SUMMARY A case is described of the successful use of intravenous glyceryl trinitrate in controlling ischaemia-induced high-grade ventricular ectopic activity occurring in a patient during a Prinzmetal angina attack. The intravenous form of glyceryl trinitrate is probably more effective than the sublingual form in controlling arrhythmias arising during acute ischaemic episodes because of prompt delivery of the drug to the coronary circulation where vasodilatation occurs. In addition, the ability to control the quantity and rate of drug delivery with an intravenous infusion offers distinct advantages in cases of coronary spasm occurring during situations such as coronary arteriography where it can be administered with careful electrocardiographic and haemodynamic monitoring.

In 1959, Prinzmetal described the clinical syndrome of variant angina pectoris characterised by distinct ST segment elevations on the electrocardiogram and a high incidence of ventricular arrhythmias (Prinzmetal et al., 1959). Coronary artery spasm has been documented in these patients and is presumed to be the cause of such attacks in a substantial percentage of patients (Oliva et al., 1973). The performance of coronary arteriography on patients with coronary spasm may be associated with a higher than normal risk of ventricular arrhythmias including ventricular fibrillation (MacAlpin, 1976; Yasue et al., 1974). We report here the successful use of intravenous glyceryl trinitrate during arteriography for the treatment of severe myocardial ischaemia and ventricular ectopic activity in a patient with Prinzmetal angina.

Case report

The patient is a 51-year-old white man, previously in excellent health, who developed severe retrosternal chest pressure while chopping wood. He was admitted to the coronary care unit of a local community hospital where he was asymptomatic for 72 hours; serum cardiac enzyme levels were normal, and electrocardiograms were interpreted as within normal limits (Fig. 1a). He subsequently developed spontaneous recurrent bouts of severe retrosternal chest pain associated with pronounced (22 mm) ST segment elevation in leads V1–5 of the electrocardiogram (Fig. 1b). Each episode of pain and electrocardiographic abnormality was relieved within several minutes by sublingual glyceryl trinitrate, though the pain recurred in 5- to 6-hour cycles. With most episodes of chest pain, ventricular tachycardia developed at a rate of 150 beats a minute. This arrhythmia was characterised by slightly irregular runs of wide bizarre QRS complexes occurring in groups of 8 to 10 beats in a row and lasting 2 to 3 minutes. Treatment was begun with oral propranolol, 120 mg, every 6 hours; isosorbide dinitrate, 2·5 mg, sublingual, every 3 hours; and glyceryl trinitrate paste, 2·5 cm, every 4 hours. In addition, a lignocaine infusion at 1 mg/min was begun.

The patient was transferred to the Peter Bent Brigham Hospital for further evaluation. On admission, his physical examination was unremarkable except for an apical fourth heart sound. Serial electrocardiograms obtained during a pain-free interval were unchanged compared with that shown in Fig. 1a.

The day after admission, the patient underwent cardiac catheterisation. Before selective coronary arteriography could be performed, he complained of chest pain and an electrocardiographic monitor (lead II) showed distinct ST segment depression and ventricular ectopic activity (Fig. 2). Sublingual glyceryl trinitrate, 0·3 mg, was administered and, because of worsening ventricular ectopic activity, lignocaine, 100 mg, was given as an intravenous

Fig. 1a *Electrocardiogram during a pain-free interval (1 mV = 10 mm).*
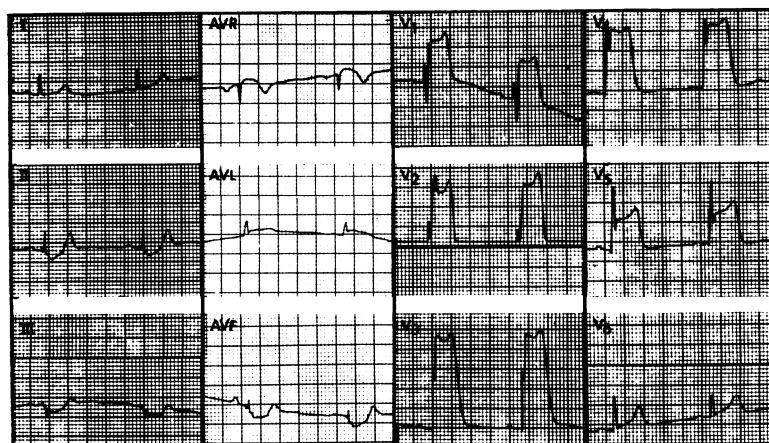

Fig. 1b *Electrocardiogram during chest pain showing distinct ST elevation in anterior praecordial leads (1 mV = 10 mm).*

bolus. The monitor rhythm strip showed an initial return of ST segments to baseline with abolition of ventricular ectopic activity. However, ST segment shift recurred, accompanied by high-grade ventricular ectopic activity including runs of ventricular tachycardia. In order to obtain prompt relief of the ischaemia-induced arrhythmias, 100 µg glyceryl trinitrate was administered intravenously as a bolus.

Fig. 3 shows the time course of reversal of the electrocardiographic abnormalities. Within 60 seconds, the ST segments had returned toward baseline and ventricular ectopic activity had disappeared. Within 120 seconds after the administration of intravenous glyceryl trinitrate, the QRS-T configuration had become normal.

Coronary arteriograms were then performed during a continuous intravenous infusion of glyceryl trinitrate at 5 to 10 µg/min and showed isolated stenosis, greater than 90 per cent, of the proximal left anterior descending coronary artery. Left ventriculography showed minimal anterior wall hypokinesis. A saphenous vein aortocoronary artery bypass graft to the left anterior descending coronary artery was performed immediately after cardiac catheterisation, and the patient subsequently had
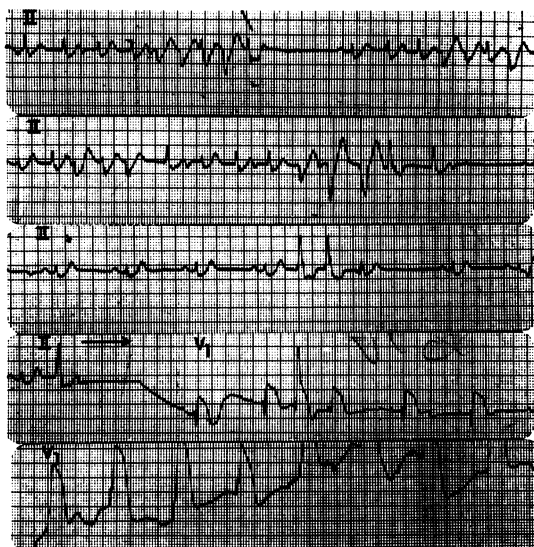
Fig. 2 *Rhythm strip obtained in the catheterisation laboratory during the first episode of angina. The lead was changed from II to V_1 in the 4th strip as noted. The tracings show sinus rhythm with ST segments consistent with acute ischaemic injury, alternating with sinus pauses and episodes of junctional and ventricular ectopic activity.*
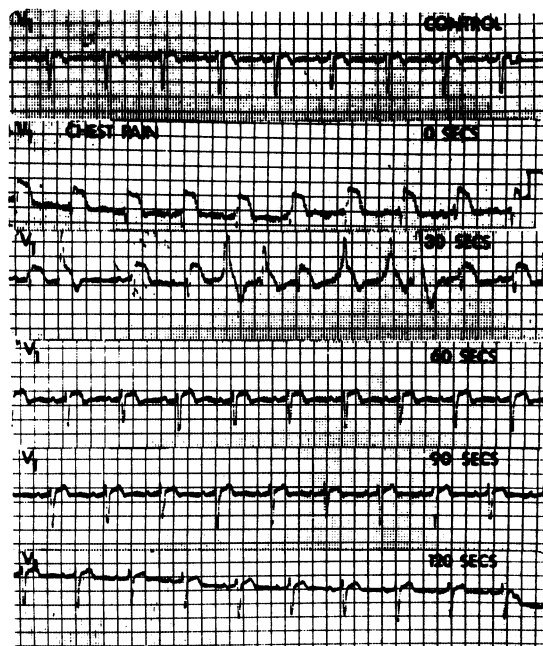

Fig. 3 *Non-continuous rhythm strips showing the time course of disappearance of ischaemic ST changes after administration of a 100 µg intravenous bolus of glyceryl trinitrate at time 0 seconds.*

an uneventful postoperative course. Fifteen months after operation he remains asymptomatic and has returned to work.

Discussion

This patient's clinical history, widespread typical electrocardiographic changes during chest pain, and severe proximal left anterior descending coronary artery stenosis suggest that superimposed coronary spasm resulted in ischaemia of a large region of the myocardium. The profound degree of coronary artery spasm demonstrated in several recent reports has been shown to result in conspicuous reduction, if not total obliteration, of coronary blood flow to a large segment of myocardium (Oliva *et al.*, 1973; Endo *et al.*, 1976). Recently, Maseri and co-workers (1978) have documented coronary artery spasm causing myocardial infarction when superimposed on vessels with a 90 per cent luminal stenosis.

Severe ischaemic injury to myocardial cells has been shown to result in ventricular arrhythmias. Bigger *et al.* (1977) have summarised the possible mechanisms of ventricular arrhythmias arising in the early (less than 15 minutes) arrhythmic phase of the Harris model of myocardial infarction in the dog. As a result of ischaemia, there is partial or complete inactivation of the fast inward sodium channel, raised extracellular potassium, lowered intracellular pH, and partial depolarisation of the injured cells. The action potentials generated by partially inactivated fast sodium currents and catecholamine enhanced slow inward calcium currents promote re-entry leading to ventricular tachycardia and ventricular fibrillation.

Conventional antiarrhythmic agents may have little, if any, success in controlling arrhythmias associated with acute ischaemia. Hope *et al.* (1974) have shown in the acutely ischaemic dog model that neither lignocaine nor procainamide was effective in reducing the time of onset of ventricular tachycardia after coronary occlusion. In a study of 2-hour-old canine infarcts, Kupersmith *et al.* (1975) showed that the beneficial effect of lignocaine in eliminating the dispersion of refractoriness between normal and ischaemic myocardium occurred with a delayed time course after drug administration. This lack of effectiveness of those agents may be the result both of an impairment of delivery to the ischaemic myocardium and inappropriate electrophysiological effects upon the ischaemic cells.

Our patient had received 200 mg subcutaneous lignocaine for local anaesthesia in addition to a continuous infusion of lignocaine at 1 mg/min and an acute intravenous bolus of 100 mg at the onset of

ventricular tachycardia. Therefore, ventricular tachycardia recurred with myocardial ischaemia in spite of presumably high myocardial levels of lignocaine. The ability of intravenous glyceryl trinitrate to reverse coronary spasm (Schroeder *et al.*, 1977) and restore blood flow serves to eliminate many of the above pathological factors contributing to early phase ischaemia-induced arrhythmias, and probably contributed to rapid arrhythmia control in our patient. Epstein and colleagues (1973) reported dramatic improvement in arrhythmias when glyceryl trinitrate was administered in acute experimental or clinical myocardial infarction. Presumably as a result of increased myocardial perfusion the ventricular fibrillation threshold in acutely ischaemic dog hearts was increased, and the incidence of ventricular premature contractions in patients soon after admission to the coronary care unit with myocardial infarction was decreased (Epstein *et al.*, 1973, 1975).

Although other vasodilators such as nitroprusside have been shown to have directionally similar gross haemodynamic changes, glyceryl trinitrate has the advantage of increasing regional myocardial blood flow to ischaemic zones. This may occur through its greater vasodilator effect on large coronary conductance vessels as compared with small coronary resistance vessels (Chiariello *et al.*, 1976).

Glyceryl trinitrate is usually administered by the sublingual route. However, intravenous glyceryl trinitrate is probably more effective than the sublingual form of the drug in quickly controlling ischaemia-induced ventricular ectopic activity in view of its rapid onset of action (less than 60 seconds in this patient) because of prompt delivery of the drug to the coronary circulation. In addition, the ability to control the quantity and rate of drug delivery with an intravenous infusion offers distinct advantages. In this patient, a continuous intravenous infusion of glyceryl trinitrate was helpful in controlling ischaemia and arrythmias for a prolonged period of time, allowing coronary arteriogrraphy to be performed safely. Further studies will be necessary to document its safety and effectiveness, but this agent seems particularly well suited for cases of coronary spasm encountered during angiography when it can be administered with careful electrocardiographic and haemodynamic monitoring, to control potentially life-threatening ischaemia and arrhythmias.

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